REMARKS

Reconsideration and reexamination of the subject application are respectfully requested in light of the foregoing amendments and following remarks.

The amendments to the claims are supported throughout the specification as filed and do not enter new matter into the application. The amendments correct informalities or more clearly set forth the nature of the claimed invention, for the reasons set forth below. Amendments are made without prejudice or disclaimer of subject matter that Applicants may claim in a subsequently filed continuing application.

1. Status of the Claims; Request for clarification on the status of claim 36

Claims 1-29 are canceled. Claims 30-38 are pending. Withdrawn claims 32, 36, and 38 are canceled by the present amendment. Claims 30, 31, 33-35, and 37 stand rejected.

2. Traverse of the Restriction Requirement

Claim 32 of Group II, as well as the other withdrawn claims, are canceled by the present amendment, making the grounds for traverse moot.

3. Status of the Drawings

The drawings filed on April 10, 2004, are deemed acceptable by the Examiner.

4. Acknowledgement of the Certified Priority Documents

Applicants note with appreciation the acknowledgement of the certified priority documents.

5. Acknowledgement of Information Disclosure Statement

Applicants note with appreciation the acknowledgement of the Information Disclosure Statement filed March 9, 2006.

6. Objection to the Claims

Claims 33 and 37 are objected to as directed to a non-elected invention. Withdrawn claims 32, 36, and 38 are canceled by the present amendment, and the dependencies of claims 33 and 37 are amended accordingly. The objections thus are moot.

The Office also objects to claims 30, 34, and 35 for informalities. The claims are presently amended according to the Examiner's recommendations, and the objections should be withdrawn.

7. Rejection Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 30-31, 33-35, and 37 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants traverse the rejection as it applies to the amended claims.

The Office interprets "*a* nucleotide sequence of SEQ ID NO: 1" as reading on *any* nucleotide sequence of SEQ ID NO: 1, e.g., a fragment thereof. Office Action, page 3. This language is found at part (1) of claim 30, and the rejection is based solely on the Office's interpretation of this one element of claim 30. The Office does not make a case—as it must—that any other element of claim 30 is inadequately described. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992) (the Office bears the burden of showing an inadequate written description). The present amendment clarifies that part (1) of claim 30 is directed to "An isolated polynucleotide comprising . . . the nucleotide sequence of SEQ ID NO: 1." This claim element is presently expressed in language similar to the other elements of claim 30. The nucleotide sequence of SEQ ID NO: 1 is adequately described in the specification, as admitted by the Office at the bottom of page 3 of the Office Action. The rejection accordingly may be withdrawn.

8. Rejection under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 30-31, 33-35, and 37 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner specifically alleges that none of the claimed subject matter is enabled. Applicants traverse the rejection as it applies to the amended claims.

As the Office indicates, enablement is determined by weighing several factors to determine whether undue experimentation would be required to make or use the claimed invention. *See In re Wands*, 858 F.2d 731, 736, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). The amount of experimentation to practice the full scope of the claimed invention is not undue, if the experimentation is routine in nature and the techniques necessary to perform the experimentation are well known to the skilled artisan. *See, e.g., Johns Hopkins Univ. v.*

Cellpro, Inc., 152 F.3d 1342, 1360, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) ("test [for undue experimentation] is not merely quantitative . . . if it is merely routine"); *Falkner v. Inglis*, 448 F.3d 1357, 79 U.S.P.Q.2d 1001 (Fed. Cir. 2006) ("The person of ordinary skill in the art would clearly have possessed such knowledge, and given the ready accessibility of the journals, the absence of incorporation by reference is not problematic."); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986) (A "patent need not teach, and preferably omits, what is well known in the art.").

In the present case, contrary to the various allegations in the Office Action at page 6, the specification provides ***working examples*** of the claimed invention. The invention relates to a CYP90D1 gene (SEQ ID NO: 1) controlling the final step of brassinosteroid synthesis in combination with a ROT3 gene (residues 51-1625 of SEQ ID NO: 3). *See, e.g.*, Specification, page 1, first paragraph. The specification discloses both the CYP90D1 and ROT3 proteins and nucleic acids encoding these proteins. *See, e.g.*, Sequence Listing. The specification discloses that the inventors previously disclosed a method of modulating the expression of ROT3 to alter the morphology of leaves and flowers. *See, e.g.*, Specification, page 2, first paragraph. The inventors have shown that the expression of both CYP90D1 and ROT3 in a whole plant is effective to alter the morphology of not just leaves and floral organs, but the whole plant. *See, e.g.*, Specification, page 5, third paragraph; page 10, third paragraph. The specification provides a working example of plants that have knock-out mutations of the ROT3 gene or the ROT3 and CYP90D1 genes, which provides evidence of the function of these genes in brassinosteroid synthesis. *See, e.g.*, Specification, page 11, third paragraph, through page 13, third paragraph. The specification discloses a working example of the nucleic acids encoding CYP90D1 and ROT3; various nucleic acids, such as plasmids, comprising the nucleic acids (*e.g.*, Specification, page 11, last paragraph, through page 12, second paragraph); and the use of these nucleic acids to alter the morphology of a plant by transforming the plant with the nucleic acids (*e.g.*, Specification, page 13, third paragraph). The specification provides promoters, vectors, and transforming methods for this purpose that are used routinely by the skilled artisan for this purpose. *See, e.g.*, Specification, page 6, last paragraph, through page 7, fifth paragraph. In short, the Office has provided no evidence, as it must, that undue experimentation would be required to make and use the claimed nucleic acids, and it has ignored considerable contrary evidence in the specification, including working examples. The rejection accordingly should be withdrawn.

Further, the Office has provided no evidence that undue experimentation would be required to make and use the CYP90D1 and ROT3 proteins with one amino acid deletion, substitution, or addition, where the protein stimulates brassinosteroid biosynthesis, as claimed. Amino acid alterations can be made to the proteins having the sequences of SEQ ID NO: 2 or SEQ ID NO: 4 by standard molecular biological procedures, such as oligonucleotide-directed mutagenesis. The present disclosure provides the complete sequence of nucleic acids encoding these proteins, so the experimentation required to make a mutation to the encoding nucleic acids is routine. The specification further provides knock-out plants in which the variant CYP90D1 and ROT3 nucleic acids can be expressed using routine methodology and assayed for gain of function in brassinosteroid biosynthesis. *See, e.g.*, Specification, page 6, last paragraph, through page 7, fifth paragraph; page 13, third paragraph.

The skilled artisan was aware that ROT3 proteins encoded by a *rot3* allele, *rot3-2*, displayed the same biological activity as wild-type ROT3. *Rot3-2* has a point mutation that results in the replacement of Gly-80 by Glu in a proline-rich domain of the ROT3 protein. The ROT3-2 protein encoded by the *rot3-2* allele, however, produces the same phenotype as the wild-type ROT3. *See* Kim *et al.*, *Proc. Nat'l Acad. Sci. USA* 96: 9433-37 (August 1999) at page 9435, left col. Kim is cited on an IDS, filed herewith.

Further guidance to make the appropriate amino acid modifications is provided by the 51% sequence conservation between CYP90D1 and ROT3. *See, e.g.*, Specification, page 2, lines 13-20. The artisan generally understands that protein function is more likely to be affected by modifying conserved amino acid residues. The skilled artisan further appreciates that limited amino acid alterations, *e.g.*, a single amino acid modification, generally can be made with a reasonable expectation of maintaining protein function. Gassner *et al.*, *Proc. Nat'l Acad. Sci USA* 93: 12155-58 (1996) ("Gassner") provided in an IDS filed herewith, reveals that considerable (up to 10) amino acid alterations can be made even to the tightly packed core of a globular protein without eliminating activity or folding of the protein. Wells, *Biochemistry* 29: 8509-17 (1990) ("Wells"), also provided in the IDS, discloses that the free energy changes in mutant proteins generally are additive with increasing numbers of amino acid mutations. Wells shows that proteins generally function when they have single, or even multiple, amino acid changes. Wells states:

> [R]emoval of a single molecular contact by a point mutation causes relatively small reductions (typically 0.5-5 kcal/mol) in the free energy of transition-state destabilization, protein-protein interactions, or protein stability compared to the overall free energy associated with these functional properties (usually 5-20 kcal/mol).

Wells, page 8509, left col. (citations omitted). This means that a protein typically can be modified at one or several amino acid positions without loss of their functional properties. Wells also concludes that the effect of most mutations on structure is highly localized, and thus less likely to affect function. Wells, page 8516, left col. In the present case, a single amino acid alteration is well within the limits that proteins typically can tolerate while retaining function, as evidenced by Gassner and Wells, for example. The proteins with altered sequences that are encompassed by the claims thus would thus be reasonably expected to retain biological function, and only routine experimentation would be required to identify those proteins without biological activity. 35 U.S.C. § 112, first paragraph, does not require disclosure of a test with *every* species covered by a claim, even in an unpredictable art. *In re Angstadt*, 537 F.2d 498, 502, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). Further, some experimentation to determine which embodiments encompassed by the claims will work is permitted without the experimentation being undue in nature. *See Angstadt*, 190 U.S.P.Q. at 218; *Wands*, 858 F.2d 736-37 ("Enablement is not precluded by the necessity for some experimentation such as routine screening."). For all the foregoing reasons, the claims are enabled by the specification, and the rejection may be withdrawn.

9. Rejection under 35 U.S.C. § 102(b)

Claims 30-31 and 33 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kim *et al.*, *Genes Devel.* 12: 2381-91 (1998) ("Kim"). Applicants traverse the rejection.

Kim discloses the nucleotide sequence of SEQ ID NO: 4, which encodes the ROT3 protein. ROT3 and variants thereof are encoded by the nucleotide sequence recited in part (3) of claim 30.

Claim 30 *additionally* requires *inter alia* an isolated polynucleotide comprising (1) the sequence of SEQ ID NO: 1. The Office contends that Kim additionally discloses part (1) of claim 30, because the Office interprets "a nucleotide sequence of SEQ ID NO: 1" to read broadly on ROT3. The present amendment clarifies that part (1) of claim 30 instead is directed to "An isolated polynucleotide comprising . . . the nucleotide sequence of SEQ ID

NO: 1." Because Kim does not teach this element, Kim does not anticipate claim 30. The rejection accordingly should be withdrawn.

10. Rejection of the Claims Under 35 U.S.C. § 101

Claims 30, 31, 34, 35, and 37 are rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. Applicants traverse the rejection.

Claim 30 and dependent claims 31, 34, 35, and 37 are presently amended to recite an "isolated" polynucleotide, as recommended by the Examiner, so the rejection can be withdrawn.

CONCLUSION

Should the Examiner have any questions or comments regarding Applicants' response, he is asked to contact Applicants' undersigned representative at (202) 842-8862. Please direct all correspondence to the below-listed address.

In the event that the Office believes that there are fees outstanding in the above-referenced matter and for purposes of maintaining pendency of the application, the Office is authorized to charge the outstanding fees to Deposit Account No. 50-0573. The Office is likewise authorized to credit any overpayment to the same Deposit Account Number.

Respectfully submitted,

Date: September 25, 2007

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